Sleep Medicine 15 (2014) 269–272

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Brief Communication

Prevalence of residual excessive sleepiness during effective oral appliance therapy for sleep-disordered breathing

A.E.R. Verbruggen [a,f,*], M. Dieltjens [a,b,f], K. Wouters [c], I. De Volder [d,e], P.H. Van de Heyning [a,d,f], M.J. Braem [b,f], O.M. Vanderveken [a,d,f]

[a] ENT Department and Head and Neck Surgery, Antwerp University Hospital, Antwerp, Belgium
[b] Department of Special Care Dentistry, Antwerp University Hospital, Antwerp, Belgium
[c] Scientific Coordination and Biostatistics, Antwerp University Hospital, Antwerp, Belgium
[d] Multidisciplinary Sleep Disorders Centre, Antwerp University Hospital, Antwerp, Belgium
[e] Department of Neurology, Antwerp University Hospital, Antwerp, Belgium
[f] Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

ARTICLE INFO

Article history:
Received 28 May 2013
Received in revised form 4 October 2013
Accepted 1 November 2013
Available online 30 December 2013

Keywords:
Obstructive sleep apnea
Mandibular advancement device
Epworth Sleepiness Scale
Daytime sleepiness
Dental sleep medicine
Sleep disordered breathing

ABSTRACT

Background: Oral appliance therapy with a mandibular advancement device (OA_m) can yield to complete therapeutic response (apnea–hypopnea index [AHI] < 5 events/h), though some patients show little or no improvement in daytime sleepiness. The prevalence of residual excessive sleepiness (RES) despite effective treatment with OA_m therapy is unknown. We aimed to determine the prevalence of RES in patients treated with a titratable custom-made duobloc OA_m.

Methods: A prevalence study was performed, collecting data from 185 patients with an established diagnosis of sleep-disordered breathing (SDB) under OA_m therapy with a titratable custom-made duobloc device (baseline data were male:female ratio, 129:56; age, 48 ± 9 years; body mass index [BMI], 27 ± 4 kg/m^2; Epworth Sleepiness Scale [ESS] score, 10 ± 5; and AHI, 19 ± 12 events/h). A full-night polysomnography was performed at baseline and after 3 months of OA_m therapy. Daytime sleepiness was assessed using the ESS with RES defined as an ESS score of 11 or higher out of 24, despite complete therapeutic response.

Results: Out of 185 patients, 84 patients (45%) showed a complete therapeutic response with an AHI of <5 events per hour after 3 months of OA_m therapy. Despite this normalization of AHI, 27 out of these 84 patients (32%) showed RES and had a significantly higher baseline ESS (15 ± 4 vs 9 ± 4; $P < .001$) and were younger (43 ± 9 vs 47 ± 9; $P = .028$) compared to patients without RES.

Conclusion: RES under OA_m therapy showed a prevalence of up to 32% in SDB patients effectively treated with respect to AHI. Patients with RES were younger and had higher baseline daytime sleepiness.

1. Introduction

Sleep-disordered breathing (SDB) is a highly prevalent public health issue affecting 9–24% of the middle-aged population [1]. It spans a wide pathophysiologic continuum of severity, ranging from snoring over obstructive sleep apnea (OSA) to obesity hypoventilation syndrome [2]. OSA is the most common type of SDB and is characterized by recurrent episodes of partial or complete collapse of the upper airway, resulting in intermittent hypoxemia, hypercapnia, and disruption of the normal sleep pattern [3]. The consequences associated with undiagnosed or untreated SDB include excessive daytime sleepiness (EDS), cardiovascular morbidity, reduced quality of life, and increased risks for motor vehicle and occupational accidents [1].

Continuous positive airway pressure (CPAP) is the current standard of therapy for moderate to severe OSA [4]. However, its clinical effectiveness is limited by poor patient acceptance and tolerance and unsatisfactory compliance [5]. Oral appliances are considered to be the main alternative to CPAP therapy for patients with mild to moderate OSA and for patients who do not comply with or refuse long-term CPAP treatment [6]. Within the group of oral appliances, the most commonly prescribed is the type of oral appliance that brings the mandible in a protruded position during sleep (OA_m). The aim of this treatment is to prevent upper airway collapse by increasing the cross-sectional pharyngeal area, thereby reducing snoring and OSA. The use of OA_m therapy has been reported to be effective in reducing patients' hypersomnolence [6]. However, a number of patients show little or no improvement in

* Corresponding author at: Antwerp University Hospital (UZA), Wilrijkstraat 10, 2650 Edegem, Antwerp, Belgium. Tel.: +32 (0)3 821 34 36; fax: +32 (0)3 821 42 71.
E-mail address: annelies.verbruggen@uza.be (A.E.R. Verbruggen).

1389-9457/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.sleep.2013.11.781

daytime sleepiness despite complete response with OA_m therapy for SDB severity. The prevalence of residual excessive sleepiness (RES) under OA_m-therapy currently is unknown. Therefore, the aim of our study was to explore the prevalence of RES during effective OA_m therapy.

2. Methods

Our cross-sectional single-center study evaluated the prevalence of RES in SDB patients treated with a titratable, custom-made OA_m. For the evaluation of daytime sleepiness, the Epworth Sleepiness Scale (ESS) was used. The ESS is a self-administered well-validated questionnaire that measures how likely patients are to fall asleep in eight different sedentary situations, previously determined to be soporific. Total ESS scores range from 0 to 24. Scores of $\geqslant$11 or $\geqslant$16 are indicative of EDS or severe EDS, respectively [7,8].

Baseline ESS and anthropomorphic and polysomnographic data were collected for 185 consecutive SDB patients treated with a custom-made, titratable OA_m (Resident Butterfly, Dormoco, Belgium [9] (n = 143) or SomnoDent Flex, Somnomed AG, Australia [10] (n = 42). The characteristics of the patients are shown in Table 1. All patients were evaluated at baseline and reevaluated after 3 months of OA_m therapy, including a full-night polysomnography with the OA_m in situ. Effective treatment was defined as a complete response with a reduction of apnea–hypopnea index (AHI) to less than five events per hour [11]. The other patients were considered as nonresponders. Ethical approval for our study was obtained from the institutional review boards of the Antwerp University Hospital.

2.1. Statistics

Data were statistically analyzed using SPSS (SPSS version 17.0, SPSS Inc, Chicago, Illinois, USA). Descriptive statistics for clinical characteristics of patients were presented as mean ± standard deviation (SD). The significance level was set at .05. Normality of distribution was assessed using Q–Q plots and the Shapiro–Wilk normality test. Continuous data between groups were compared with an unpaired t test if the data were normally distributed and with the nonparametric Mann–Whitney U test if the data were not. A paired t test or Wilcoxon signed-rank test were used to

Table 1
Patient characteristics. Bold values represent statistically significant values (P < .05)

Variable	All patients (n = 185)	Complete responders (n = 84)		P value
		RES (n=27)	Non-RES (n=57)	RES vs non-RES
Men (n; %)	129; 70%	16; 59%	37; 65%	.295
Age (y)	47.7 ± 8.9	42.7 ± 8.7	47.4 ± 8.9	**.028**
Baseline				
BMI (kg/m^2)	26.8 ± 4	26.1 ± 3.8	26.2 ± 3.4	.818
ESS (mean ± SD; range)	10 ± 5.1; 1–20	14.5 ± 3.6; 7–19	8.6 ± 4.4; 1–20	**<.001**
AHI (events/h)	19.1 ± 12.2	13.6 ± 16.9	14.9 ± 9.8	.981
Sleep efficiency (%)	83.4 ± 10.4	86.1 ± 9.3	82.4 ± 10.9	.08
TST (min)	384.5 ± 61.6	395.1 ± 61.4	381.4 ± 72.6	.4
St N1 (%TST)	6.8 ± 4.4	6.8 ± 3.4	7.8 ± 5.1	.85
St N2 (%TST)	51.4 ± 12.1	51.1 ± 13.3	48.7 ± 10.8	.13
St N3 + N4 (%TST)	20.4 ± 10.4	19.8 ± 13.4	22.1 ± 8.9	.06
St REM (%TST)	19.7 ± 6.2	21.9 ± 7.8	19.8 ± 5.8	.2
Time awake (min)	53.8 ± 46.1	43.7 ± 33.8	57.2 ± 49.4	.28
LMI (events/h)	21.1 ± 21.9	17.7 ± 15.9	17.9 ± 15.0	.9
PLMI (events/h)	13.5 ± 18.6	14.0 ± 15.8	11.2 ± 12.9	.6
ODI (events/h)	6.3 ± 7.5	3.4 ± 4.2	4.0 ± 4	.3
Mean saturation (%)	95.1 ± 1.4	95.6 ± 1.6	95.4 ± 1.2	.6
Minimum saturation (%)	85.1 ± 8.1	87.5 ± 6.7	86.3 ± 7.1	.3
With OA_m				
BMI (kg/m^2)	27.0 ± 4.0	26.3 ± 4.0	26.1 ± 3.4	.365
ESS (mean ± SD; range)	7.9 ± 4.6	14.0 ± 2.6	5.4 ± 2.9	**<.001**
AHI (events/h)	9.3 ± 9.4	2.5 ± 1.7	2.6 ± 1.3	.445
Sleep efficiency (%)	82.9 ± 11	83.0 ± 10.3	84.2 ± 9.6	.5
TST (min)	385.7 ± 58.1	380.7 ± 53.5	388.8 ± 55.3	.5
St N1 (%TST)	6.1 ± 3.8	6.2 ± 3	5.9 ± 3.7	.5
St N2 (%TST)	52.1 ± 11.1	55.3 ± 9.7	50.7 ± 11.3	.11
St N3 + N4 (%TST)	20.4 ± 9.3	17.1 ± 7.5	22.7 ± 10.0	**.01**
St REM (%TST)	21.3 ± 6.4	21.4 ± .6.8	20.7 ± 6.5	.7
Time awake (min)	52.3 ± 43.7	60.1 ± 42.1	45.3 ± 36.8	.06
LMI (events/h)	19.9 ± 21.6	18.1 ± 3.4	16.6 ± 17.4	.7
PLMI (events/h)	11.4 ± 15.9	10.9 ± 16.2	10.0 ± 14.7	.8
ODI (events/h)	3.2 ± 3.7	1.1 ± 0.9	1.4 ± 1.1	.1
Mean saturation (%)	95.1 ± 1.3	95.8 ± 1.3	95.1 ± 1.3	**.035**
Minimum saturation (%)	87.6 ± 4.9	89.6 ± 3.9	88.5 ± 4.9	.2
Δ AHI (events/h)	9.7 ± 11.7	11.0 ± 6.9	12.2 ± 9.8	.97
Subjective compliance (d/wk)	6.6 ± 1.1	6.9 ± 0.5	6.6 ± 1.1	.1
Subjective compliance (h/night)	6.9 ± 1.1	6.8 ± 1.2	7 ± 0.7	.4
Adjusted subjective compliance (%)	96.7 ± 11.4	100 ± 0	99.3 ± 13.5	.51

Abbreviations: RES, residual excessive sleepiness; OA_m, mandibular advancement device; y, year; BMI, body mass index; ESS, Epworth Sleepiness Scale; SD, standard deviation; AHI, apnea–hypopnea index; h, hour; TST, total sleep time; min, minutes; St, sleep stage; REM, rapid eye movement; PLMI, periodic limb movement index; LMI, limb movement index; ODI, oxygen desaturation index; d, day; wk, week.
RES: AHI OA_m < 5 events/h and ESS OA_m $\geqslant$ 11.
Non-RES: AHI OA_m < 5 events/h and ESS OA_m < 11.
Adjusted compliance: mean rate of OA_m use corrected for subjective TST.
Data are presented as mean ± SD unless otherwise stated.

compare measurements at baseline and at evaluation with OA_m. To assess differences in gender composition, a χ^2 analysis was used. We dichotomized age (cutoff, 45 years) and baseline ESS (cutoff $\geqslant$11/24) and calculated the crude odds ratios (ORs) of having RES and the OR adjusted for the other dichotomized variable, together with their 95% confidence intervals (CI). The Spearman rank correlation coefficient was used to calculate the correlation between change in AHI and change in ESS.

3. Results

In the cohort of 185 consecutive SDB patients treated with a custom-made titratable OA_m, 45% (n = 84) had a complete response (male:female ratio, 52:32; age, 45.9 ± 9.1 years; body mass index [BMI], 26.2 ± 3.5 kg/m^2; AHI, 14.4 ± 8.9 events/h) and 101 patients were nonresponders (male:female ratio, 77/24; age, 49.3 ± 8.5 years; BMI, 27.3 ± 4.3 kg/m^2; AHI, 22.9 ± 13.2 events/h).

Twenty-seven (32%) out of the 84 patients with a complete response under OA_m exhibited RES having an ESS score of $\geqslant$11. Eight of these 27 patients showed severe RES with an ESS score of $\geqslant$16. In 12 of the RES patients, confounding factors were identified, such as depression, restless legs syndrome, periodic limb movement disorder, narcolepsy, or intake of medication influencing vigilance resulting in 15 patients (18%) out of 84 who remained sleepy without any other evident explanation.

As shown in Table 1, the mean ESS score of the 27 patients with RES was 14.0 ± 2.6 despite complete response under OA_m therapy, which was similar to baseline (14.5 ± 3.6; P = .525). Patients with RES had a significantly higher baseline ESS (14.5 ± 3.6 vs 8.6 ± 4.4; P < .001) and a younger age (42.7 ± 8.7 vs 47.4 ± 8.9; P = .028) than non-RES patients (complete response and ESS score of <11).

The OR of RES was 9.9 (95% CI, 3.0–32.4; P < .001) when baseline ESS scores were 11 or higher out of 24 and 4.1 (95% CI, 1.5–10.7; P = .004) when age was younger than 45 years. When ESS was adjusted for age, the OR was 8.5 (95% CI, 2.5–28.8; P = .001), and the OR was 3.2 (95% CI, 1.1–9.3; P = .03) when age was adjusted for ESS. The interaction between both parameters was not significant (P = .197). The Spearman rank correlation coefficient between change in AHI and change in ESS was not significant (ρ = .009; P = .93).

4. Discussion

To our knowledge, our study is the first to provide data about the prevalence of RES in SDB patients undergoing OA_m therapy. The results of our study showed that the prevalence of RES under effective OA_m therapy (AHI of <5 events/h) ranged from 18% to 32% depending on the definition. Patients with RES were younger and had a higher baseline ESS than those without RES.

The prevalence of RES during CPAP treatment as mentioned in literature varies from 6% to 16% [12–14], which is similar to the prevalence of 18% found in an unselected general population study [15]. These values were lower than the results reported in our study. Our population was slightly younger than those reported on in the other studies [12–14]. Because our results showed that patients with RES were younger as also demonstrated by Pepin et al. [12], the factor of age could be important to explain the difference found in the prevalence of RES. In addition, our study contained no exclusion factors, and therefore the population was most likely less homogeneous with more confounding factors. Therefore, we hypothesize that the composition of the study population is of major importance in describing the prevalence of RES in SDB patients treated with OA_m.

The subjective compliance was high and no significant difference in subjective compliance between RES and non-RES patients could be demonstrated. Measures of objective compliance are lacking. However, a high level of agreement between objective and subjective compliance data was recently reported [16].

Our results showed a significant difference in sleep architecture between both groups regarding the percentages of deep sleep with less deep sleep in RES patients vs non-RES patients. This finding could help to explain the excessive sleepiness in RES patients. The results also showed a statistically significant difference in mean blood oxygen saturation, though this small difference might be considered as not clinically relevant.

The results of our study were based on subjective measurement of daytime sleepiness. There is much controversy in the literature regarding the most accurate method to assess sleepiness and both objective and subjective methods have their limitations [17–19]. Objective measures do not replace the ESS method but could provide an added value.

Because of the known negative impact of RES on daily functioning and quality of life [20], these patients have to be carefully followed up and possible causes of RES have to be evaluated and treated when possible. Based on the results of our study, further prospective research is required concerning the prevalence of and the possible causes leading to RES during OA_m therapy. Additionally, possible treatments of this condition need to be studied using objective testing of daytime sleepiness.

5. Conclusion

Our results of this first ever calculation showed that the prevalence of RES under effective OA_m ranges from 18% to 32%. Patients with RES were younger and had higher baseline daytime sleepiness, as measured using the ESS.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2013.11.781.

Funding sources

This work was supported by the Agency for Innovation by Science and Technology, Flanders, Belgium (IWT), project number 090864.

References

[1] Young T, Palta M, Dempsey J, Skatrud J, Weber J, Badr J. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–5.
[2] Piper AJ, Grunstein RR. Obesity hypoventilation syndrome: mechanisms and management. Am J Respir Crit Care Med 2011;183:292–8.
[3] Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999;22:667–89.
[4] Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1981;1:862–5.
[5] Grote L, Hedner J, Grunstein R, Kraiczi H. Therapy with nCPAP: incomplete elimination of sleep-related breathing disorder. Eur Respir J 2000;16:921–7.
[6] Kushida CA, Morgenthaler TI, Littner MR, Alessi CA, Bailey D, Coleman J, et al. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: an update for 2005. Sleep 2006;29:240–3.
[7] Oksenberg A, Arons E, Nasser K, Shneor O, Radwan H, Silverberg DS. Severe obstructive sleep apnea: sleepy versus nonsleepy patients. Laryngoscope 2010;120:643–8.

[8] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540–5.
[9] Dieltjens M, Vanderveken OM, Hamans E, Verbraecken JA, Wouters K, Willemen M, et al. Treatment of obstructive sleep apnea using a custom-made titratable duobloc oral appliance: a prospective clinical study. Sleep Breath 2013;17:565–72.
[10] Gotsopoulos H, Chen C, Qian J, Cistulli PA. Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial. Am J Respir Crit Care Med 2002;166:743–8.
[11] Phillips CL, Grunstein RR, Darendeliler MA, Mihailidou AS, Srinivasan VK, Yee BJ, et al. Health outcomes of continuous positive airway pressure versus oral appliance treatment for obstructive sleep apnea. a randomized controlled trial. Am J Respir Crit Care Med 2013;187:879–89.
[12] Pepin JL, Viot-Blanc V, Escourrou P, Racineux JL, Sapene M, Lévy P, et al. Prevalence of residual excessive sleepiness in CPAP-treated sleep apnoea patients: the French multicentre study. Eur Respir J 2009;33:1062–7.
[13] Stradling JR, Smith D, Crosby J. Post-CPAP sleepiness—a specific syndrome? J Sleep Res 2007;16:436–8.
[14] Nguyen XL, Rakotonanahary D, Chaskalovic J, Philippe C, Hausser-Hauw C, Lebeau B, et al. Residual subjective daytime sleepiness under CPAP treatment in initially somnolent apnea patients: a pilot study using data mining methods. Sleep Med 2008;9:511–6.
[15] Pallesen S, Nordhus IH, Omvik S, Sivertsen B, Tell GS, Bjorvatn B. Prevalence and risk factors of subjective sleepiness in the general adult population. Sleep 2007;30:619–24.
[16] Dieltjens M, Braem MJ, Vroegop AV, Wouters K, Verbraecken JA, De Backer WA, et al. Objectively measured vs. self-reported compliance during oral appliance therapy for sleep-disordered breathing. Chest 2013;144:1495–502.
[17] Johns MW. Sensitivity and specificity of the multiple sleep latency test (MSLT), the maintenance of wakefulness test and the Epworth Sleepiness Scale: failure of the MSLT as a gold standard. J Sleep Res 2000;9:5–11.
[18] Chervin RD, Aldrich MS. The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnea. Neurology 1999;52:125–31.
[19] Santamaria J, Iranzo A, Ma Montserrat J. Persistent sleepiness in CPAP treated obstructive sleep apnea patients: evaluation and treatment. Sleep Med Rev 2007;11:195–207.
[20] Weaver TE, Chasens ER, Arora S. Modafinil improves functional outcomes in patients with residual excessive sleepiness associated with CPAP treatment. J Clin Sleep Med 2009;5:499–505.